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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/932,370	08/17/2001	Mitchell Shirvan	62812-A/JPW/GJG/CSN	4884

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EXAMINER	
HUI, SAN MING R	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/932,370	Applicant(s) SHIRVAN ET AL.	
	Examiner San-ming Hui	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-96* is/are pending in the application.

4a) Of the above claim(s) *4,5,25,28,29,50,51,74 and 75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-24,26,27,30-49,52-73 and 76-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Applicant's election with traverse of the specie, N-(2-n-propylpentanoyl) glycinamide, in Paper No. 6 is acknowledged. The traversal is on the ground(s) that no serious burden would be imposed onto the office because the compounds of Formula I and II only differ by one double bond. This is not found persuasive because the basis of the specie election requirements set forth in the previous office action, mailed August 27, 2002, is not based on the structural differences between the compounds of Formula I and Formula II. The ground and reason of specie election requirement is that, as discussed in the previous office action mailed august 27, 2002, the compounds recited in the claims can be classified in vastly different subclasses in class 514, for example, 616, 613, 617, 247+, and 211, depending upon what moieties attached to the core structure. With aromatic or heterocyclic moieties attached to the core structures of Formula I or II, the classification of the compounds changes because aromatic or heterocyclic compounds are well recognized as different fields of art as they behave vastly different chemically and pharmacologically than their non-aromatic counterparts. The search is not only limited to patent file. Therefore, the search for all species encompassed by the claims would impose a serious burden of search to the Office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-96 are pending.

Claims 4, 5, 25, 28, 29, 50, 51, 74, and 75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected specie,

there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

The claims have been examined herein to the extent they read on the elected invention and species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-92, 94, and 96 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for headache, migraine, and neuropathic pain, does not reasonably provide enablement for other type of pain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In the instant case, the claims are directed to a method of preventing pain by employing the herein claimed valproic acid derivative. The specification discloses the method of treating allodynia by employing the herein claimed compound. However, the specification fails to adequately teach how to use the method to prevent such pain. The only example discussing preventing of pain is experimental example 2, page 17-19 in the instant specification. However, this example only demonstrates the efficacy of treating allodynia (a painful condition) when the animals have already suffered from

pain. No example is set forth in the instant specification on prevention of pain by employing the herein claimed compounds before pain occurred. The term "pain" encompasses conditions with vastly different etiologies, such as trauma, surgery, neuropathic, infection, and even psychological origins. Applicants have not provided any convincing evidence that their claimed invention is indeed useful as preventive for **all** pain and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-29, 47-92, 94, and 96 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 26-29 and 72-75 recite the limitation "R_4" in line 2. There is insufficient antecedent basis for this limitation in the claim.

The expression, "a method of preventing pain" in claim 47, 94, and 96, renders the claims indefinite as failing to clearly set forth the metes and bounds of the patent protection desired. Examples of how and when to prevent pain are not set forth in the specification. The only example discussing preventing of pain is experimental example 2, page 17-19 in the instant specification. However, this example only demonstrates the efficacy of treating allodynia (a painful condition) when the animals have already

suffered from pain. No example is set forth in the instant specification on prevention of pain by employing the herein claimed compounds before pain occurred. Absent such exemplication, the skilled artisan could not establish the identity of those situations wherein prevention of pain would be effected. Furthermore, it is unclear as to the degree of prevention (e.g., total prevention, some prevention, probable prevention, total prevention in most cases...etc.) herein because the specification does not disclose the extent of prevention achieved. Examiner would favorably consider the term "prophylaxis" over "prevention".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 6-24, 26, 27, 30-49, 52-73, and 76-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bialer et al. (US Patent 5,585,358 from the IDS

received April 22, 2002) in view of Hansen (Southern Medical Journal, 1999;92(7):642-649), McQuay et al. (BMJ, 1995;311:1047-1052), Shank et al. (US Patent 5,760,007), Carrazana et al. (US Patent 6,319,903), Magnus (Epilepsia, 1999;40(Suppl 6):S66-S72), and Zakrzewska et al. (Pain 1997;73(2):233-230).

Bialer et al. teaches the elected compound, N-(2-n-propylpentanoyl) glycinamide, is useful as anticonvulsant for treating epilepsy and other neurological disorders (see the abstract, and col. 7, line 23-44, Example 1; col. 13, line 4 – col.17, line 34). Bialer et al. teaches the effective dose in a composition for N-(2-n-propylpentanoyl) glycinamide as 10 to about 500mg (col. 3, line 59-61). Bialer et al. also teaches the ED_{50} dosage of N-(2-n-propylpentanoyl) glycinamide for antiepileptic activities as 73mg/kg (about 5000mg in an 70kg adult) (See col. 13, line 39). Bialer et al. also teaches N-(2-n-propylpentanoyl) glycinamide can be administered through oral, intravenous, intraperitoneal, intramuscular, and topical (See col. 7, line 10-14). Bialer et al. also teaches those skilled in the art would be able to determine the precise effective amount and routes of administration of the herein compound to be administered (See col. 6, line 49-59).

Bialer et al. does not expressly teach N-(2-n-propylpentanoyl) glycinamide to be useful as treating or preventing acute, chronic, and neuropathic pain. Bialer et al. does not expressly teach the dosage of N-(2-n-propylpentanoyl) glycinamide as 6000mg or 3000mg. Bialer et al. does not expressly teach the route of administration as intranasal, sublingual, inhalation, buccal, intravaginal, and pulmonary. Bialer et al. does not

expressly teach the dosing frequency of N-(2-n-propylpentanoyl) glycinamide as periodic six times daily.

Hansen teaches various antiepileptic agents are useful in treating both acute and chronic pain (See page 642, col. 2, second paragraph, page 646, col. 2, fourth paragraph to page 647, whole page).

McQuay et al. teaches the effectiveness of various anticonvulsants such as carbamazeoine, phenytoin, Valproate sodium are effective in treating neuropathic pain such as trigeminal neuralgia and migraine prophylaxis in various degree (See the abstract, Tables 1-4, also Section Trigeminal neuralgia and Migraine prophylaxis).

Shank et al. teaches topiramate, an anticonvulsant, is useful in treating neuropathic pain (See claim 2).

Carrazana et al. teaches topiramate, an anticonvulsant, is useful in treating cluster headaches (See claims 1-15).

Magnus teaches gapapentin, an anticonvulsant, is useful in treating neuropathic pain and useful in migraine prophylaxis (See Summary, also page S66 to S68, first col. Second paragraph; also page S71, Table 5).

Zakrzewska et al. teaches lamotrigine, an anticonvulsant, is useful in treating trigeminal neuralgia, a neuropathic pain. (See the abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ N-(2-n-propylpentanoyl) glycinamide, in the herein claimed dosage and dosing regimen, in a method of treating and prophylaxis pain. It would have been obvious to one of ordinary skill in the art at the time the invention was

made to administer N-(2-n-propylpentanoyl) glycinamide in the herein claimed routes of administration.

One of ordinary skill in the art would have been motivated to employ N-(2-n-propylpentanoyl) glycinamide, in the herein claimed dosage and dosing regimen, in a method of treating and prophylaxis pain. Based on the cited prior art, antiepileptic compounds with vastly different structure and mechanism of actions are useful for treating and preventing neuropathic pain, migraine headache and cluster headache. The only common property of these antiepileptic compounds is that they are all useful as anticonvulsant. Therefore, employing any known anticonvulsant, including the N-(2-n-propylpentanoyl) glycinamide, would have been reasonably expected to be useful to treat or prevent neuropathic pain, migraine headache and cluster headache. Furthermore, the optimization of result effect parameters (e.g., dosage range, dosing regimens) is obvious as being within the skill of the artisan, based on the teachings of Bialer et al. (See col. 6, line 49-59).

One of ordinary skill in the art would have been motivated to administer N-(2-n-propylpentanoyl) glycinamide in the herein claimed routes of administration because one of ordinary skill in the art would be charge to possess all the conventional method of administering a therapeutic compound. Selecting the herein claimed routes of administration over the obvious alternatives would be considered obvious as being within the purview of a skilled artisan.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-

1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
December 27, 2002

SREENI PADMANABHAN
PRIMARY EXAMINER

12/30/02